The court went on to consider recent cases that had led to some confusion in this area and reviewed the **University of California v. Eli Lilly** 43 USPQ2d 1398, **Gentry Gallery v. Berkline** 45 USPQ2d 1498 and **Enzo Biochim v. Gen-Probe** 63 USPQ2d 1609 cases. The court noted that the first of these had held that description of DNA if insulin in one species did not constitute a written description of the gene for all other species based on the state of the art at the relevant time and that the third had held that a functional definition might meet the requirement of the law if in the knowledge of the art the disclosed function is sufficiently correlated to a particular known structure. It then held that both of these were "inapposite in the present case because the claim here was not to new or unknown biological material .that ordinarily skilled artisans would easily miscomprehend". So far as **Gentry Gallery** was concerned, on its proper reading this stood for nothing more that the well established principle that "a broadly drafted claim must be fully supported by the written description and drawings". That decision had therefore not created any new rule that a claim might be invalid simply on the ground that it failed to include an essential element.

Form this analysis, it seems clear that, at least in cases such as the present where there is clear verbal support in the original disclosure of the language that is being employed in the claims that the test is whether the skilled reader of the description would recognize that what is being claimed is a) understandable and b) defines the same invention as is described (the latter requirement including the requirement that the inventor was in possession of the invention as the Examiner notes was the holding of the **Vas-Cath** case she cites, although this is not the only reason, as was pointed out in the **Enzo Biochemcase** noted above). While the breadth of the claim may be relevant to these questions, the court is backing away from the interpretation that some have put on its earlier decisions arguing that only limited claim scope is permissible in the field of biotechnology. Such views are clearly refuted by the latest **Amgen** decision

In the present case, what is claimed is a chimeric protein in which the nature of fifteen different domains is specified. The examiner has given no reason why one skilled in the art would have any difficulty in knowing what is required of these domains and, as noted above, when this requirement is met, a functional definition of a claim feature should be permissible.

Page 3 of the present description sets out the background against which the question of whether what is claimed represents the same invention as what is described. From this background, it seems clear that one skilled in the art should appreciate that selection of appropriate domains provides a means for achieving the desired result, namely membrane spanning proteins that can pass particular signals into a cell. . Claim 1 defines appropriate domains for this purpose.

There is a strong presumption that an adequate written description is present in the specification as filed (**in re Wertheim**, 541 F.2d, 257, 262 (CCPA 1976), and the Examiner has not met the burden of showing the contrary. The Examiner's rejection appears to be based on her view that a person of ordinary skill in the art would not be able to identify the domains specified in the pending claims and that a specific sequence is necessary to satisfy 35 USC Section 112, first paragraph . Applicants do not agree. The precise location of domains with an NPY receptor, as with other G protein-coupled receptors, can be readily determined by routine computer analysis (as described in the specification at page 1, line 16 to page 2, line 21). The specification further provides specific domain locations for NPY1 and NPY5 receptors chimeras are provided in SEQ ID Nos: 6, 9, 10 and 20-27. Based on this disclosure, the metes and bounds of each recited domain and the present claims are readily understood as defining the invention described.

The Examiner further asserts that the claims must recite a "clearly-defined amino acid sequence (e.g., SEQ ID NO:9)," and appears to interpret this requirement as meaning that polypeptide claims must be limited to a particular amino acid sequence. Applicants do not agree. It is well established that an applicant need not specifically disclose every species encompassed by the claims. For example, a description of a genus of genetic material may be achieved by providing a representative number of sequences or by reciting common structural features. **University of California v. Eli Lilly**): see also MPEP Section 2163. Applicants have done both, providing 11 representative sequences and a detailed description of the structural features common to these sequences and to the remainder of the genus. Accordingly, Applicants submit that this ground for rejection has been overcome.

Claims 1-9 further stand rejected under 35 USC Section 112, second paragraph, for lack of enablement. In particular, the Examiner is of the view that the specification does not describe the precise functional characteristics of the chimeric receptors encompassed by the present claims.

The Applicants also traverse this rejection. As an initial matter, we do not understand the Examiner"s statement that "the specification does not teach functional or structural characteristics of the chimeric NPY receptor polypeptide recited in the claims" (page 6). The chimeric receptors recited in the present claims bind NPY receptor ligand, as described in Example 5, and GTP, as described in Example 6. The structural characteristics, as noted above, are spelled out in the specification in great detail, and each polypeptide comprises all fifteen specific domains in the recited order and without intervening amino acids. Thus, both functional and structural characteristics are provided in the specification. Those of ordinary skill in the art could readily make the chimeras of the present invention, and use them in assays of receptor binding and/or function (e.g., for identifying compounds that bind to NPY5 as described, for example, in the specification at page 23, lines 7-25).

The Examiner then points out that protein structure, by itself, is insufficient to determine protein function. To support this point, the Examiner cites several references that question the ability to determine the function of a previously unknown, naturally occurring protein based on structural similarity to a known protein. Applicants do not disagree with the Examiner on this point, but believe that this discussion is irrelevant to the present issue. Applicants are not using the structure of an unknown protein to determine function; rather the present chimeric proteins are made up of well characterized sequences who functions have already been determined. All NPY receptors bind GTP and NPY receptor ligand (e.g., NPY or PYY). Applicants have demonstrated that chimeric NPY receptors in which a limited number of particular domains are replaced with the corresponding domain from a different species or a different NPY receptor subtype retain both of these functions. Thus, the function of the present chimeras is not predicted based solely on structure. Accordingly, Applicants believe that it would not require undue experimentation to make and use the chimeric polypeptides of the present invention.

It is therefore submitted that the application meets both the written description and enablement requirement of 35 USC 112.

It is therefore submitted that the application is now in order for allowance and an early action this end is respectfully submitted.

Respectfully submitted,

John Richards
Reg. No. 31053
Ladas & Parry
26 W. 61st Street
New York, NY 10023
(212) 708-1915

Appendix

The paragraph starting at page 2 line 3:

> GPCRs have been structurally modeled as to secondary and tertiary structural conformation, and the precise locations of the extracellular, TM and intracellular domains within their primary structures (i.e., their amino acid sequences) are well known and generally agreed to in the art (see, e.g., Baldwin, *EMBO J.* 12:1693-703, 1993, ~~also see http://swift.embl-heidelberg.de/7tm/seq/snakes.html~~). These receptor proteins thus comprise an extracellular N-terminal domain, seven membrane-spanning alpha helical domains (connected by three intracellular loop domains alternating with three extracellular loop domains), and an intracellular C-terminal domain.

The paragraph starting at page 2 line 11:

> The locations of the various domains of NPY receptors can be readily determined by inspections of the "Viseur's snake like view" for the particular receptor polypeptide generated by the European Molecular Biology Laboratory's Viseur software. These Viseur's snake like views are electronically published for a wide variety of GPCR polypeptides (including NPY receptors of various mammalian and non-mammalian vertebrate species ~~--http://swift.embl-heidelberg.de/7tm/seq/snakes.html~~). In these snake like views, the amino acids of the polypeptide sequence of the receptors are set forth as one-letter-code-containing circles. The TM domains are depicted as diagonally stacked circles to represent the alpha helical conformation believed to be adopted by of these domains in situ, while the other domains are depicted as vertically and horizontally arrayed sequences.

The paragraph starting at page 5 line 30:

> The NPY5 receptor has been suggested to play a key role in the modulation of feeding behavior. Studies of seizure-prone mice have led to the suggestion that the Y5 receptor may also have an anti-epileptic activity in the control of limbic seizures. Y5-like receptors have also been implicated in attenuation of morphine withdrawal symptoms, enhancement of diereses and natriuresis, lowering of blood glucose, inhibition of luteinizing hormone secretion, and reduction of acetylcholine release in the ileum. See, for example, Hu, et al., *J. Biol. Chem.*, 271:26315-19, 1996; Gerald, et al., *Nature*, 382:168-71, 1996; Blomqvist, et al., *TINS*, 20: 294-98, 1997. The sequences of Y1 and Y5 receptors of humans, dogs, mice, guinea pigs, rats, and Y1 receptors of sheep have all been reported and have been published, e.g., by Genbank ~~(http://www.ncbi.nlm.nih.gov/)~~.

the paragraph starting at page 6 line 24 by the following:

> In the human Y1 receptor (DNA sequence - SEQ ID NO:1, amino acid sequence - SEQ ID NO:2), the third intracellular loop domain consists essentially of amino acids 232

(Phe) to 263 (Ile) of SEQ ID NO:2, as indicated, for example, by the Viseur's snake like view for this receptor ~~(see, e.g., http://swift.embl-heidelberg.de/7tm/seq/vis/NY1R_HUMAN/NY1R_HUMAN.html)~~. In accordance with the amino acid sequence residue charge/polarity considerations discussed above, the termini of this loop are preferably defined by the presence (within the domain) of a charged residue (Lys 233 of SEQ ID NO:2) located at the end of the long stretch of hydrophobic residues (the fifth TM domain) and a charged residue (Arg 260 of SEQ ID NO:2) located at the beginning of the long stretch of hydrophobic residues (the sixth TM domain).

The paragraph starting at page 7 line 3 :

In the rat Y1 receptor, the third intracellular loop domain consists essentially of amino acids 231 (Phe) to 262 (Val) of SEQ ID NO:3, as indicated, for example, by the Viseur's snake like view for this receptor ~~(see, e.g., http://swift.embl-heidelberg.de/7tm/seq/vis/NY1R_RAT/NY1R_RAT.html)~~. In accordance with the amino acid sequence residue charge/polarity considerations discussed above, the termini of this loop domain are preferably defined by the presence (within the domain) of a charged residue (Lys 232 of SEQ ID NO:3) located at the end of the long stretch of hydrophobic residues (the fifth TM domain) and another charged residue (Arg 259 of SEQ ID NO:3) located at the beginning of the long stretch of hydrophobic residues (the sixth TM domain).

The paragraph starting at page 7 line 12:

The following discussion of human NPY5 domains illustrates the domain structure information available electronically for this receptor ~~(see, e.g., http://swift.embl-heidelberg.de/7tm/seq/vis/NY5R_HUMAN/NY5R_HUMAN.html)~~.